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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,748	10/27/2005	Alejandro Merino	085449-0159	6988

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EXAMINER	
LEE, JAE W	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,748	MERINO ET AL.	
	Examiner	Art Unit	
	Jae W. Lee	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-56* is/are pending in the application.

4a) Of the above claim(s) *46-48,55 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

In the preliminary amendment for claims, filed on 10/27/2005, Applicants have cancelled Claims 1-45 and added new Claims 46-56.

Claims 46-56 are pending in this application.

Priority

A claim of priority to the PCT/EP03/07848, filed on 07/18/2003, Foreign Application EPO 02016110.5, filed on 07/19/2002, and Foreign Application EPO 03101321.2, filed on 05/12/2003, is acknowledged.

Election

Applicant's election with traverse of Group II (screening method, claims 49-54), SEQ ID NOs: 10 and 15 is acknowledged. The traversal is on the ground(s) that the search and examination of Group I and II is not unduly burden to the examiner and that the MPEP states a "reasonable" number of sequences can be examined in one application, e.g., up to 10 sequences.

In response to Applicant's traversal, the Examiner finds Applicants' arguments not persuasive because the inventions of Group I and II have acquired a separate status in the art, are related as product and process of use and classified differently, i.e. Group I drawn to a product and Group II to a method, therefore, literature and sequence

searches required for each of the Group is not required for another thereby presenting a search burden on the Examiner should the groups be examined together.

Also, each SEQ ID No: # corresponds to a structurally and functionally different polypeptide having different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01), and they are not obvious variants of each other. Furthermore, sequence searches do not overlap, and they are not coextensive. In addition, as Applicant's have noted, MPEP does state that a "reasonable" number of sequences can be examined is "up to 10 sequences," and the examination of 2 SEQ ID Nos is "up to 10 sequences." Therefore, Applicants' argument is not found persuasive as stated above.

It is also noted by the Examiner that Claims 55 and 56 are drawn to a method of treatment. They were originally restricted to be included in Group I (see previous office action). Therefore, since the subject matter of Applicant's election of Group II is drawn to a method of screening, Claims 55 and 56 are withdrawn from further consideration as being drawn to a non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 46-48, 55 and 56 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 49-54 will be examined on the merits as they read on the elected species (i.e. SEQ ID Nos: 10 and 15).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Objections to the Oath or Declaration

A new oath or declaration is required because of following informalities. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: the declaration filed on 10/27/2005 contains incorrect filing date for Foreign Application EPO 02016110.5 and fails to reference Foreign Application EPO 03101321.2, filed on 05/12/2003.

Claim Objections

Claims 49-54 objected to because of the following informalities:

Claim 49 (50-54 dependent therefrom) is objected to because it depends from a non-elected Claim 46.

Claim 49 (50-54 dependent therefrom) is objected to because it contains the recitation of non-elected inventions, i.e. (a) and (b) drawn to SEQ ID NO: 4 and SEQ ID NO: 11 respectively. As such, the limitations recited in (a) and (b) of Claim 49 will be

withdrawn from further consideration as being drawn to non-elected species (see above Election).

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-54 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 49-54 are directed to a method of screening for a molecule that binds either to the protein complex of HDAC1 and SWI/SNF complex 60 kDa subunit or to any of its protein components ; the method comprising the steps of (a) exposing the complex or any protein component or any cell or any organism containing the complex or any protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or any protein component.

It is noted by the Examiner that the phrase, "protein component(s)" recited in Claims 49-54, is interpreted broadly to be any single amino acid residue because

Applicant's elected invention (Claims 49-54) depends from Claim 46 which recites "a protein complex comprising (v) based upon the recitation of Claim 46 (v) "HDAC1" (SEQ ID No:10), *a functionally active derivative thereof, a functionally active fragment thereof, a homolog thereof, or a variant of "HDAC1" encoded by a nucleic acid that hybridizes to the "HDAC1" nucleic acid or its complement under low stringency conditions*, and (viii) "SWI/SNF COMPLEX 60 KDA SUBUNIT" (SEQ ID No:15), *a functionally active derivative thereof, a functionally active fragment thereof, a homolog thereof, or a variant of "SWI/SNF COMPLEX 60 KDA SUBUNIT" encoded by a nucleic acid that hybridizes to the "SWI/SNF COMPLEX 60 KDA SUBUNIT" nucleic acid or its complement under low stringency conditions* (italicized to illustrate how broad the Claims are).

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of [compositions or methods], it must be clear that: (1) the identifying characteristics of the claimed [compositions or methods] have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

The specification discloses a general protocol for isolation of TAP-tagged protein complexes. This is an inadequate written description for a method of screening for a molecule that binds either to the protein complex of HDAC1 and SWI/SNF complex 60 kDa subunit or to any of its protein components; the method comprising the steps of (a) exposing the complex or any protein component or any cell or any organism containing

the complex or any protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or any protein component.

Claim 49 is drawn to a method for screening for a molecule that binds the protein complex of Claim 46 or to any of its protein components, comprising the steps of (a) exposing the complex, any protein component, any cell or any organism containing the complex or any protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or any protein component. However, Applicants' claim does not recite a structure (i.e., SEQ ID NOs: 10 and 15) for claimed methods comprising the use of the complex or any protein component, and the specification does not provide a disclosure of any particular structure to function/activity relationship in the protein complex or any protein component.

Given the lack of additional representatives of a method for screening for a molecule that binds the protein complex of Claim 46 or to any of its protein components, the method comprising the steps of (a) exposing the complex, any protein component, any cell or any organism containing the complex or any protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or any protein component, as encompassed by the claim, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 49-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for a method for screening for a molecule that binds to a protein complex comprising SEQ ID NO: 10 and SEQ ID NO: 15 via purification methods using Tandem Affinity Purification (TAP), does not reasonably provide enablement for a method of screening for a molecule that binds either to a protein complex of Claim 46 or to any of its protein components; the method comprising the steps of (a) exposing the complex or any protein component or any cell or any organism containing the complex or any protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or any protein component. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not

'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Claims 49-54 are so broad as to encompass any method of screening for a molecule that binds either to a protein complex of Claim 46 or to any of its protein components; method comprising the steps of (a) exposing the complex or any protein component or any cell or any organism containing the complex or any protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or any protein component.

The claims rejected under this section of U.S.C. 112, first paragraph, do not place any structural limits on the claimed method comprising screening molecules that bind "protein complex," "complex" or "protein component." Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which amino acid residues in a protein can be used while obtaining the desired function

requires a knowledge of and guidance with regard to which amino acids in the peptide's sequence, if any, are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the peptide's structure relates to its desired function. In addition, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methods comprising screening molecules that bind many different peptides/proteins. The specification, however, only discloses only two peptides, i.e. SEQ ID NO: 10 and 15.

The specification does not support the broad scope of the claims which encompass methods comprising determining whether a molecule can bind to all modifications and fragments of any protein complex, any protein component, any cell or any organism because the specification does not establish: the claimed methods, wherein (A) regions of any protein complex or any protein component structure which may be modified without affecting its desired function, i.e. histone deacetylase or chromatin remodeling activity; (B) the general tolerance of any protein complex or any of its protein component to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of any protein complex or any of its protein component with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Because of this lack of guidance, and the fact that the relationship between the amino acid sequence of a protein and its activity/function is not well understood and unpredictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary

Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to make and use encompass a method of screening for a molecule that binds either to a protein complex of HDAC1 and SWI/SNF complex 60 kDa subunit or to any of its protein components; method comprising the steps of (a) exposing the complex or any protein component or any cell or any organism containing the complex or any protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or any protein component.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of claimed methods comprising screening molecules that bind to any protein complex or any protein component having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 49-54 are rejected under 35 U.S.C. § 102(b) as being anticipated by Underhill et al. (A Novel Nuclear Receptor Corepressor Complex, N-CoR, Contains Components of the Mammalian SWI/SNF Complex and the Corepressor KAP-1, J. Biol. Chem., Vol. 275, Issue 51, 40463-40470, December 22, 2000).

The instant claims are drawn to a method for screening for a molecule that binds either to the protein complex of claim 46 or to any of its protein components; the method comprising the steps of: (a) exposing the complex or protein component, or a cell or organism containing the complex or protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or protein component.

It is noted by the Examiner that the phrase, "protein component(s)" recited in Claims 49-54, is broadly but reasonably interpreted to include a single amino acid residue. The reason is that the "protein component(s)" is of "a protein complex comprising (v) HDAC1 (SEQ ID No:10), *a functionally active derivative thereof, a functionally active fragment thereof, a homolog thereof, or a variant of HDAC1 encoded by a nucleic acid that hybridizes to the HDAC1 nucleic acid or its complement under low stringency conditions*, and (viii) SWI/SNF COMPLEX 60 KDA SUBUNIT (SEQ ID No:15), *a functionally active derivative thereof, a functionally active fragment thereof, a homolog thereof, or a variant of SWI/SNF COMPLEX 60 KDA SUBUNIT encoded by a nucleic acid that hybridizes to the SWI/SNF COMPLEX 60 KDA SUBUNIT nucleic acid or its complement under low stringency conditions* as recited in Claim 46, from which

Applicant's elected invention (Claims 49-54) depends from (italicized to illustrate how broad the Claims are, see also 112 1st paragraph rejection above).

Underhill et al. teach the isolation of two multiprotein nuclear receptor corepressor (N-CoR) complexes, designated N-CoR-1 and N-CoR-2. Underhill et al. specifically teach the methods of purification of the N-CoR Complexes from forty liters of HeLa cells, immunoprecipitation, Western blot analysis, and mass spectroscopy to determine binding partners or complexes of N-CoR protein complexes. As shown in the Figures 2 and 6 of immunoprecipitation and Western blot analysis results in addition to the mass spectroscopy analysis in Tables 1 and Figure 3, Underhill et al. identified HDAC1, HDAC2, HDAC3 and SWI/SNF complexes (including BRG1, BAF 170, BAF 155, BAF 47/INI1) bound to the N-CoR complexes. Therefore, Underhill et al. exposed the complexes HDAC1 and SWI/SNF, or any of its protein component (see 112 2nd paragraph rejection above) to N-CoR complexes and determined their binding, thereby anticipating Applicant's Claim 49 complex was HDAC3.

Further, Underhill et al. teach the histone deacetylase activity assay by (1) isolating said protein complexes from forty liters of HeLa cells, (2) contacting HDAC1, HDAC2, HDAC3 and SWI/SNF complexes in the presence of N-CoR Complexes with a substrate of the complex, [^{3}H]histones, and (3) measuring the modulation of histone deacetylase activity of the aforementioned protein complexes (see Figure 6 C and also Experimental procedures under the section heading "*Histone Deacetylase Activity*"), thereby anticipating Claim 51.

In addition, Underhill et al. teach that purified N-CoR complexes contained 10% glycerol (see Experimental procedures under the section heading "*Purification of the N-CoR Complexes*"), thereby anticipating Claim 54 (see definition of pharmaceutically acceptable carrier in paragraph [0194] of the specification).

Furthermore, Claims 50, 52 or 53 are included in this rejection because they are drawn to intended "uses" of claimed methods while having the same active steps of Claim 49 which they depend from.

Therefore, Underhill et al. anticipate the Applicants' method for screening for a molecule that binds either to the protein complex of claim 46 or to any of its protein components; the method comprising the steps of: (a) exposing the complex or protein component, or a cell or organism containing the complex or protein component, to one or more candidate molecules; and (b) determining whether the candidate molecule is bound to the complex or protein component.

Conclusion

Claims 49-54 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

The instant Office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PRIMARY EXAMINER